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ARTIFICIAL INTELLIGENCE IN DIABETES DIAGNOSIS : PIONEERING PRECISION HEALTHCARE

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Abstract

Diabetes mellitus, a chronic metabolic disorder characterized by elevated blood glucose levels, poses a significant global health burden. Timely and accurate diagnosis is crucial for effective management and prevention of complications. In recent years, artificial intelligence (AI) has emerged as a promising tool for improving the diagnostic process of diabetes. This review article provides an overview of the current state of AI applications in diagnosing diabetes, encompassing various methodologies such as machine learning, deep learning, and predictive modeling. We discuss the utilization of diverse data sources including medical images, electronic health records, genetic information, and lifestyle factors for diabetes diagnosis. Furthermore, we examine the performance, challenges, and potential future directions of AI-based diagnostic tools in clinical practice. By synthesizing existing literature and highlighting key advancements, this review aims to elucidate the role of AI in enhancing the accuracy and efficiency of diabetes diagnosis, ultimately contributing to improved patient outcomes and healthcare delivery.

Keywords: Diabetes mellitus, Diagnosis, Artificial intelligence, Machine learning, Deep learning.

INTRODUCTION

Diabetes mellitus, also known as diabetes, is a group of metabolic disorders caused by high blood sugar levels. These high blood sugar levels result from problems with insulin production, insulin action, or both. There are two main types of diabetes: type 1 and type 2. Type 1 diabetes is caused by the destruction of insulin-producing cells in the pancreas, leading to an absolute insulin deficiency. Type 2 diabetes is more common and is caused by a combination of insulin resistance and inadequate insulin secretion.

In addition to general lifestyle changes, several diabetes management systems have been developed to help people with diabetes manage their disease. One of the key components of these systems is glucose metabolism prediction. Predicting blood sugar levels can help people with diabetes take appropriate action to prevent complications, such as hypoglycemia.

Several studies have used advanced data-driven techniques to develop accurate glucose metabolism prediction models. These models are needed because the relationship between blood sugar levels and factors such as medication, diet, physical activity, and stress is complex and nonlinear. Artificial neural networks (ANNs) are a type of non-linear regression model that is well-suited for modeling complex relationships. ANNs are inspired by the human brain and consist of computational elements called neurons. These neurons are connected by links with variable weights, which are adjusted during the training process. In this study, ANNs are trained using a backpropagation algorithm. The backpropagation algorithm efficiently calculates the gradient of the error function, which is used to update the weights of the ANN.

The rest of this paper is organized as follows: Section 2 reviews related work, Section 3 describes the data and the proposed ANN model, Section 4 presents the results, and Section 5 concludes the paper.

1.1. Background

1.1.1. Artificial intelligence

The term "artificial intelligence" (AI) has various interpretations across different research fields. However, it is commonly associated with the application of statistical learning techniques, modeling structures like artificial neural networks, and inference systems like Bayesian networks. Additionally, AI encompasses recommendation systems, such as expert or knowledge-based systems, and automation, including autonomous robotic systems. The overall goals of AI typically involve empowering computational agents to acquire and utilize skills within uncertain environments.

AI is gaining significant traction within the medical research community, with notable advancements in diverse medical applications. These include image-based diagnosis, such as automated detection of diabetic retinopathy; genome interpretation, such as identifying single-nucleotide polymorphisms associated with disease expression; the discovery of novel biomarkers; the interpretation of data from ubiquitous personal health devices, such as smartphone tracking of pandemic diseases; and unprecedented human-automation integration, such as robot-assisted surgery.

The evolution of AI has been continuous, and defining it with a precise definition is counterproductive to the objectives of this review. Instead, we advocate for a broader perspective on AI, adopting Russell and Norvig's four-quadrant framework. This framework contrasts AI as human intelligence (descriptive perspective) versus rational intelligence (normative perspective) along the left-right axis and AI as reasoning versus acting along the top-bottom axis. The resulting four quadrants help organize and relate the diverse range of AI-affiliated elements while enabling the inclusion of technologies like AID, which generally do not incorporate AI methods like machine learning.

Diabetes is characterized by elevated blood glucose levels caused by various underlying pathologies [6]. We will focus on three main types: type 1 diabetes (T1D), an autoimmune disorder that destroys insulin-producing cells, leading to insulin deficiency; type 2 diabetes (T2D), a progressive condition characterized by increasing insulin resistance and declining insulin secretion, often associated with adiposity-based chronic diseases; and gestational diabetes (GD), the occurrence of diabetes symptoms during pregnancy, which typically resolves after delivery. Poorly managed diabetes increases the risk of morbidity and mortality. While the American Diabetes Association (ADA) recognizes a fourth type of diabetes, secondary diabetes, this review focuses on T1D, T2D, and GD as they are the most prevalent forms.

II. LITERATURE REVIEW

This section provides a concise overview of recent ANN approaches to BGL prediction studies. In one study [7], researchers developed an ANN-based classification model to categorize diabetic patients into two groups. To enhance results, a genetic algorithm (GA) was employed for feature selection. The GA was used to determine the optimal number of neurons in the single hidden-layer model. Subsequently, the model was trained using the Backpropagation (BP) algorithm and GA, and classification accuracies were compared. The designed models were also compared with the Functional Link ANN (FLANN) and various classification systems like NN (nearest neighbor), kNN (k-nearest neighbor), BSS (nearest neighbor with backward sequential selection of feature), MFS1 (multiple feature subset), and MFS2 (multiple feature subset) for data classification accuracies.

Another study [8] investigated the application of a recurrent artificial neural network for predicting blood glucose levels (BGLs) and presented preliminary results for two insulin-dependent diabetic females. In this study, two patients regularly monitored and recorded their BGLs, insulin regimen, diet, and exercise activity in a diary for a ten-day period.

In a separate study [9], researchers aimed to predict the likelihood of developing diabetes in an individual. They employed parameters such as the number of pregnancies, glucose levels, blood pressure, skin fold thickness, insulin levels, body mass index, pedigree, and age. The database of 768 patients with these parameters was obtained from the National Institute of Diabetes and Digestive and Kidney Diseases. Using a feedforward neural network prediction model in conjunction with the backpropagation algorithm, they predicted whether a subject was at risk of developing diabetes based on the training dataset.

A pilot study [10] utilized Elman recurrent artificial neural networks (ANNs) to generate BGL predictions based on a history of BGLs, meal intake, and insulin injections. Twenty-eight datasets (from a single case scenario) were compiled from the freeware mathematical diabetes simulator, AIDA. It was observed that the most accurate predictions were made during the nocturnal period of the 24-hour daily cycle.

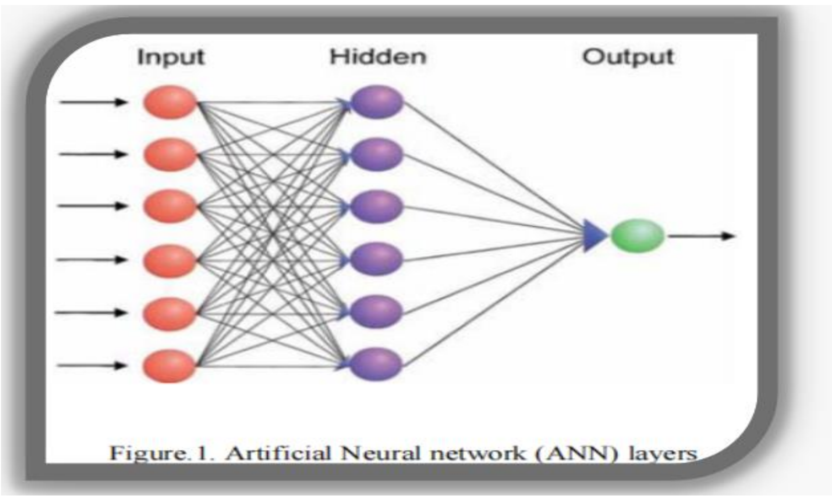


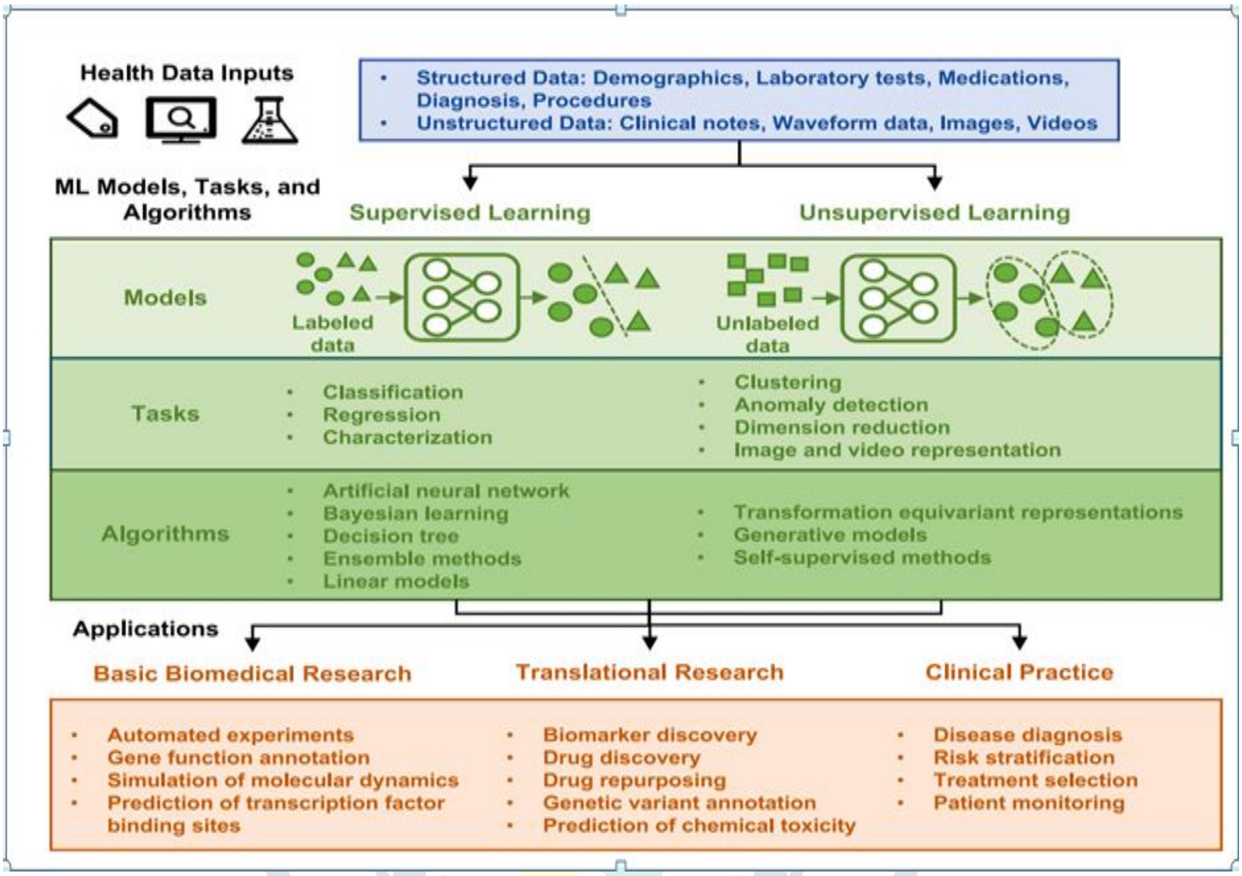
Figure.1. Artificial Neural network (ANN) layers

Overview of algorithms: Adopted from Graham et. al., 2016.

AI and improving diagnosis

The American Diabetes Association (ADA) outlines four methods for diabetes diagnosis: A1C (>6.5%), fasting blood glucose (BG) (>126 mg/dL), 2-hour oral glucose tolerance test (OGTT) (>200 mg/dL), and random BG (>200 mg/dL with classic hyperglycemia symptoms). These guidelines rely on measurements influenced by behavior and ethnicity, with suboptimal and nonsystematic cut-off values. Artificial intelligence (AI) presents an opportunity to address these limitations.

Since the early stages of type 2 diabetes (T2D) are often asymptomatic, individuals can go undiagnosed for years, potentially leading to health complications and reduced life expectancy. To address this issue and the associated costs, the diabetes research community prioritizes T2D diagnosis, exploring methods using readily



available data and non-invasive, affordable tests. These constraints encourage the development of AI-based diagnostics offering high classification accuracy and leveraging large datasets, including those from wearable and continuous monitoring devices, which are not easily interpreted without AI.

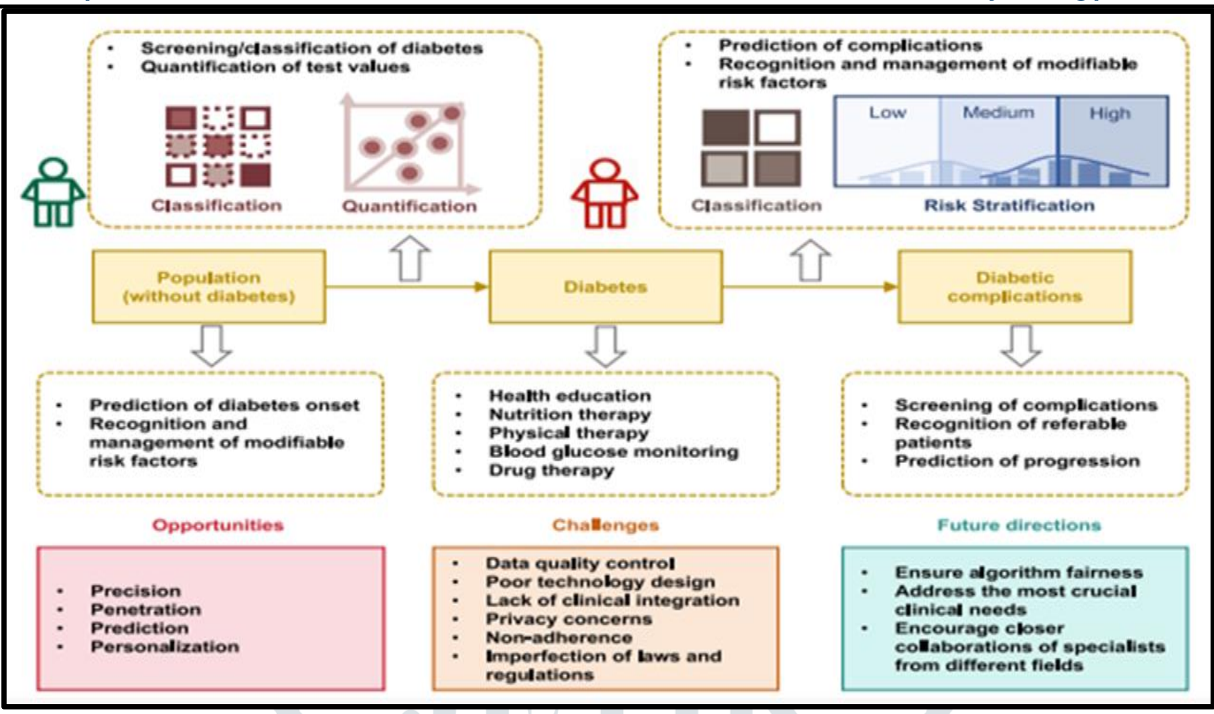
Two key study types emerged during the review process:

Maximizing Diagnostic Accuracy through AI: This approach focuses on developing AI models that achieve high accuracy in T2D diagnosis using established criteria like fasting BG or glucose tolerance.

Diagnosing with New AI-Driven Sensing Methods: This approach explores novel AI-powered sensing technologies for T2D diagnosis.

Both areas optimize diagnostics based on well-defined criteria and fall within the "rational AI" quadrants (Fig. 1). Additionally, they are action-oriented, aiming to diagnose T2D for timely treatment initiation, placing them in the "Q-RA" quadrant of Fig. 1.

Previous reviews have examined AI applications in diagnostics. Silva et al. (2023) focused on machine learning (ML) methods for T2D diagnosis, reporting area under the curve (AUC) scores ranging from 0.7 to 0.9. Logistic regression (LR) was the most popular method, but artificial neural networks (ANNs) were also explored, achieving c-indices near 0.9. Muchira et al. (2021) summarized various AI methods in the context of diagnosis, highlighting their mechanisms and potential pitfalls. This review differs from existing literature by covering a broader spectrum. Most studies compare AI methods or evaluate specific technologies from diverse datasets. To avoid inaccurate conclusions, we opted not to compare results from different studies or datasets.



Adopted from Muchira et al. (2021)

AI and managing diabetes

Artificial intelligence (AI) has been extensively researched for several decades in the context of diabetes management, driven by two main goals: (1) alleviating the significant burden placed on both patients and healthcare providers, and (2) elevating the standards of diabetes care. Numerous valuable reviews document the progress achieved in this extensive field.

Early research, summarized by Lehmann and Deutsch (2023), focused on incorporating self-monitoring blood glucose (SMBG) data, metabolic compartment models, and blood glucose observations into tools assisting clinicians in refining insulin dose calculations for type 1 diabetes (T1D) patients. As data availability and AI methods advanced, tool development progressed beyond clinician-oriented advisors to encompass patient-facing tools for managing the disease daily.

Contreras and Vehi (2018) offer a comprehensive review of AI applications in diabetes management up to 2018, covering areas such as blood glucose prediction, Artificial Insulin Delivery (AID) systems, patient and clinical decision support systems (DSS), and patient risk stratification. Their review includes helpful tables summarizing references and their scope (e.g., data types and AI methods) for a defined set of management topics.

Woldaregay et al. (2023) reviewed research on blood glucose anomaly detection, which they identified as an area not fully addressed by Contreras and Vehi. They compiled a similarly styled table of references focusing on this topic and highlighted challenges arising from the lack of accurate contextual information, such as meal and exercise data.

Two recent reviews from 2020 offer detailed discussions on T1D management and AI:

1. Tyler and Jacobs (2020) reviewed DSS, focusing on tools and systems sufficiently mature for trial implementation (both in-silico and in-vivo).
2. Vettoretti et al. (2020) reviewed DSS enabled by continuous glucose monitoring (CGM) data and AI methods for T1D. CGM technology has also facilitated the development of AID systems that automatically control insulin delivery through an insulin pump based on CGM measurements. This topic is explored further in a subsequent section.

Meal information is a crucial piece of contextual data. Qualitative trend analysis based on CGM data has demonstrated the ability to accurately identify meal timing and content, as shown in research by [53]. Similarly, machine learning techniques have been applied to the classification of daily meal and physical activity patterns, ultimately improving glucose prediction accuracy, as demonstrated in [54].

While advancements in physiological modeling, computational methods, and data acquisition have provided valuable insights into optimizing diabetes management, particularly insulin dosing regimens, the effectiveness of such management ultimately depends on patient behavior. Non-compliance with treatment, including lifestyle and behavioral recommendations, is a major factor influencing outcomes, particularly in T2D. Tsasis et al. (2023) advocate for interventions tailored to address socioeconomic determinants of health and highlight the potential of AI to identify factors that can inform such interventions.

This section features representative examples of ongoing research in the areas of prediction, patient and caregiver decision support, clinical decision support, AID systems, and patient behaviors.

TYPE 2 DIABETES MANAGEMENT

In India, where diabetes prevalence is estimated at 8-10%, with slightly higher rates in urban areas, AI/ML applications hold immense potential. Studies in Delhi found a staggering 27% prevalence rate and 46% pre-diabetes, highlighting the early and widespread occurrence of this disease. This early onset and high burden pose a significant challenge to the healthcare system, especially considering resource constraints and limited access to specialized doctors. AI/ML applications can address these challenges by bridging the gap in care and ensuring a minimum standard of treatment. A critical issue in India is the lack of uniformity in diabetes management, with primary care physicians managing numerous cases and average HbA1c levels remaining around 9%. This indicates poor control and the potential for increased complications. AI/ML approaches offer an opportunity to improve this situation.

An initiative by CCDC and AIIMS implemented a decision support system on a mobile platform to assist primary care physicians in diabetes management. However, the intervention did not show any significant improvement in glycemic control. Potential reasons for this include limited drug options, medication adjustments based on limited data points, and the lack of consideration for factors like diet, exercise, and medication adherence.

Globally, research on AI/ML algorithms for personalized diabetes therapy optimization at the patient level during routine visits is scarce, with none existing in India. Studies from China and the Western world highlight the potential of this approach. However, some caveats need consideration:

1.Data sources: Using data from various practices, while providing large datasets, may not reflect the best care standards and limit potential improvements.

2.Data noise: Multi-source data can contain high noise levels, making it difficult to identify the optimal treatment path.

3.Missing data: Lack of information on lifestyle adherence and medication compliance limits the real-world application of AI/ML models.

To overcome these challenges, future research should focus on:

- Selecting specialist practices with better-than-average glycemic control.
- Implementing careful prospective data collection, including compliance levels.
- Utilizing supervised machine learning initially, transitioning to unsupervised learning later.
- By addressing these limitations, AI/ML applications can significantly improve diabetes management in India and provide personalized, effective care for a growing population of patients.

TYPE 1 DIABETES MANAGEMENT :

While extensive research exists on applying AI/ML to type 1 diabetes, its practical implementation in India faces two major hurdles:

1. Limited adoption of insulin pumps and CGMs: Most research relies on data generated from patients using these technologies, which are not widely accessible in India due to cost constraints. This significantly limits the applicability of these findings in the Indian context.

2. Lack of comprehensive solutions: Existing research often focuses on individual aspects of type 1 diabetes management, such as food composition analysis, blood glucose prediction, or bolus calculator development. A single, integrated application or technology that addresses all essential aspects of self-management, including carbohydrate counting, insulin-carbohydrate ratio calculation, and personalized meal-based insulin dose prediction, is still missing, especially for patients on multiple daily injections (MDIs) rather than insulin pumps.

Therefore, future research aiming to improve type 1 diabetes management in India should focus on developing cost-effective solutions that can be readily implemented with MDIs and address multiple aspects of self-management in a comprehensive way

Table 1. Application of AI in predicting and screening diabetic complications

Reference	AI method	Inputs	Description	Performance
Objective: Predict the development of diabetic complications				
Lagani et al.[94]	ANN	risk factors	predicts development of diabetes-related complications	the results of the internal validation (T1D) reported a C index between 0.66 and 0.833, all statistically significantly different from 0.5 ($p \leq 0.0001$); these results were further corroborated by the external validation (49 patients with T1D), where all models obtained similarly high and statistically significant C indexes ($p < 0.05$ except for the hypoglycemia and CVD model, with $p = 0.0584$ and 0.0932, respectively); quite surprisingly, the models obtained good performance also on the T2D external cohorts, with only the neuropathy and retinopathy models achieving close to uninformative results
Marini et al.[95]	BN	risk factors	estimates long-term development and progression of complications (T1D)	the population predicted in the wrong state was below 10% on both DDO-DBN and EI-DBN
Armengol et al.[96]	case-based reasoning	risk factors	estimates risk of complications	the results were 100% correct in determining the kind of risk (progression or development) and the risk of stroke, 90% correct in determining amputation risk, and 72.45% correct in determining the global risk and the risk of infarct
Dagliati et al.[97]	RF, SVM, and LR	risk factors	predicts development of diabetes-related complications	final models, tailored in accordance with the complications, provided an accuracy up to 0.838
Khan et al.[98]	network analysis	longitudinal data	quantifies progression of comorbidities	they presented a research framework based on network theory to understand chronic disease progression along with associated comorbidities that manifest over time
Ljubic et al.[99]	RNN	hospitalization longitudinal data	predicts development of 10 selected complications (T2D)	the prediction accuracy was between 73% (myocardial infarction) and 83% (chronic ischemic heart disease), while the accuracy of traditional models was between 66% and 76%
Yang et al.[100]	LASSO regression	risk factors	estimates the risk of amputation in patients treated with canagliflozin	LASSO produced the best prediction, yielding a C index of 0.81

Overview of AI application in diabetes management: Adopted from Contreras and Vehi (2018)

Predicting process outcomes :

Blood glucose (BG) naturally fluctuates throughout the day due to food intake and insulin activity. However, factors like exercise and physical stress can also cause temporary variations. Predicting near-future BG (minutely, hourly, or overnight) is crucial for effective diabetes management and remains a vibrant research area. While BG prediction can be integrated into treatment applications (e.g., AID systems), most research focuses solely on the raw performance of generic BG predictors. This limited scope, emphasizing "rational" AI (quadrants Q-RR and Q-RA), highlights the need for human-like AI systems that translate BG predictions into meaningful therapeutic actions (e.g., insulin doses) for patients.

Contreras and Vehi (2018) compiled various prediction efforts in their review, encompassing horizons from 15 minutes to several hours. Xie and Wang (2023) compared numerous autoregressive and AI methods on a small dataset (n=6). Their evaluation did not reveal a clear winner, and AI methods did not definitively outperform autoregressive models.

Hypoglycemia prediction is particularly important due to its potential for severe complications. Kodama et al. (2023) reviewed hypoglycemia detection and prediction, concluding that no existing method is sufficiently accurate for routine use. Sevil et al. (2023) propose incorporating biosignals reflecting acute stress and physical activity into prediction algorithms, aiming for more comprehensive and accurate models**.**

AI and understanding complication:

The effectiveness of AI/ML applications relies heavily on the quality of data used to train them. While India is sometimes referred to as a "country with no records," this may be an oversimplification. It does, however, highlight the widespread lack of data recording in routine medical practice. This vast amount of untapped data holds immense potential if converted into a usable format and leveraged by AI/ML to generate insights and solutions tailored specifically to the Indian population. To unlock this potential, a concerted and collaborative effort is needed by the government and major medical associations, like the Endocrine Society of India, to initiate data collection and research initiatives.

1.Emphasizes the potential of data, rather than solely highlighting the lack of records.

2.Uses more specific and descriptive language.

3.Outlines a clear call to action for collaboration between government and medical societies.

Discussion and conclusions

Diabetes is a complex disease with varying causes, diverse presentations, and numerous confounding factors. Its management requires a growing arsenal of monitoring and treatment options. AI offers a promising solution through:

1. New data sources: Wearable devices provide personalized data specific to individual needs and populations.
2. Scalable infrastructure: Cloud computing facilitates analysis of large datasets.
3. Advances in machine learning: Powerful algorithms enable new tools for diabetes research and care.

Researchers are actively exploring AI applications in:

- Risk factor identification: Identifying individuals at risk for developing diabetes.
- Diagnosis: Improving accuracy and speed of diabetes diagnosis.
- Pathophysiology understanding: Gaining insights into the disease process and its progression.

- Disease management: Developing personalized treatment plans and monitoring strategies.

There have been notable successes, such as AI-powered diabetic retinopathy detection and closed-loop insulin delivery for T1D. However, current literature primarily focuses on best-case scenarios with high-quality, structured data.

Several limitations remain:

1) Data quality and sufficiency: Few studies address these crucial issues, even though some AI methods (e.g., deep learning) require much more data than others.
2) Data representativeness: Many studies rely on genetic sequencing and clinical data, raising questions about whether similar results can be achieved with data from consumer devices.
3) Unstructured data: Few studies attempt to analyze unstructured data like physician notes, which could provide valuable insights.
4) Imbalanced data: Learning from data with uneven class distributions remains a challenge. Evaluation metrics like AUC, sensitivity, and specificity may need adjustment for imbalanced datasets.
5) Model transferability: Studies often use small, local datasets, making it unclear whether developed models can be applied to other populations.
6) Bias and equity: Developers must ensure their models are free from systemic biases that limit their applicability and fairness. Pham et al. (2023) emphasize the importance of diverse datasets representing various ethnic and racial groups.

In conclusion, addressing data quality, sufficiency, and representativeness is crucial for the future of AI-based products in diabetes care. More prospective clinical studies are needed to address these limitations and ensure the development of truly impactful solutions.

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CONFLICT OF INTEREST:

Authors do not have any conflict of interest with any individual.

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